Wnt signaling activation: targets and therapeutic opportunities for stem cell therapy and regenerative medicine.

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Public Summary:
This review article talks about the use of small molecules that target specific proteins from a signaling pathway present in the stem cells called Wnt signaling pathway with the aim of using them to treat limbal stem cell deficiency.

Scientific Abstract:
Wnt proteins are secreted morphogens that play critical roles in embryonic development, stem cell proliferation, self-renewal, tissue regeneration and remodeling in adults. While aberrant Wnt signaling contributes to diseases such as cancer, activation of Wnt/beta-catenin signaling is a target of interest in stem cell therapy and regenerative medicine. Recent high throughput screenings from chemical and biological libraries, combined with improved gene expression reporter assays of Wnt/beta-catenin activation together with rational drug design, led to the development of a myriad of Wnt activators, with different mechanisms of actions. Among them, Wnt mimics, antibodies targeting Wnt inhibitors, glycogen-synthase-3beta inhibitors, and indirubins and other natural product derivatives are emerging modalities to treat bone, neurodegenerative, eye, and metabolic disorders, as well as prevent ageing. Nevertheless, the creation of Wnt-based therapies has been hampered by challenges in developing potent and selective Wnt activators without off-target effects, such as oncogenesis. On the other hand, to avoid these risks, their use to promote ex vivo expansion during tissue engineering is a promising application.